contraction coupling (5). Other workers have suggested that removal of calcium from its membrane site provides a site of attachment of sodium to this site, thereby producing a loss of potassium from the cell (6). Experimentally, it has been demonstrated that pentobarbital induces a decrease in potassium conductance; this decrease has been used to explain the elevation of the threshold of the fiber to direct electrical stimulation and the reduction or elimination of the action potential (7). None of these past reports have attempted a satisfactory explanation for their reported data. All imply a vague relationship between pentobarbital, potassium, and calcium. Our results similarly confirm a relationship between pentobarbital and potassium, but they permit few conclusions to be drawn. Isoantagonism implies that one agent uncouples the myocardial depressant action of the other, rendering it inert. Competition for a common receptor site would be an explanation for supra-antagonism.

Summary. The interaction between pentobarbital and increasing potassium ion concentration was investigated in isolated guinea pig atria. Each agent administered separately depressed the peak developed force of contraction. Combinations of the agents, as evaluated by isobolograms, produced isoantagonism at moderate effect levels, supra-antagonism at higher effect levels.

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A Comparison of Fetal versus Maternal Plasma Colloidal Osmotic Pressure in Man* (33809)

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The colloidal osmotic pressure (COP) measurements of maternal and fetal plasmas in sheep and goats have shown that the COP of the maternal plasma is higher than that of fetal plasma throughout gestation and that the magnitude of the difference is greater early in gestation (1). In man similar data are not available although McCarthy (2) reported COP measurements on diluted fetal plasma at term. In this study we have attempted to measure the total COP on undiluted plasma of paired human maternal and fetal plasmas collected at different stages of gestation. In addition, the discription of a rigid membrane micro-osmometer is given.

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Materials and Methods. In 33 uncomplicated full-term pregnancies in man, paired samples of fetal and maternal blood were obtained within 5 min after delivery. Fetal blood was obtained from the umbilical cord and maternal blood was obtained from the antecubital vein. Nine paired samples of maternal and fetal blood were obtained between 26 and 36 weeks of gestation following premature delivery. In addition, 10 blood samples from pregnant sheep were obtained for comparison with previous studies. The blood was collected in heparinized plastic syringes, centrifuged, and the plasma was stored at 4° until used. The COP of the plasma was measured on a 3-ml sample (large osmometer) or 0.3 ml sample (small osmometer) at room

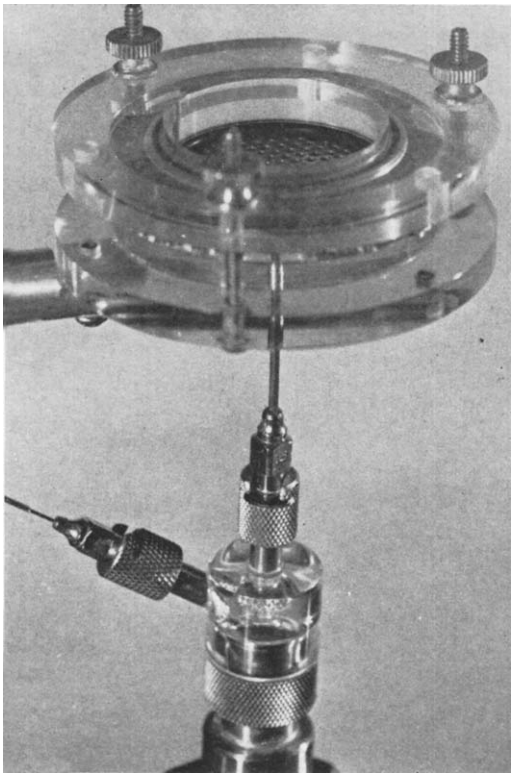

FIG. 1. Photograph of the large osmometer illustrating arrangement of stainless steel plate impregnated with collodion and Statham P23Db transducer.

temperature, 24°, and the results were corrected to body temperature, 38°, by multiplying the osmotic pressure as measured at absolute temperature T by the factor 311/T. Total plasma protein concentrations (g/100 ml) were measured colorimetrically (Biuret reaction) with a Technicon AutoAnalyzer.

The apparatus for measurement of colloidal pressure originally described by Hepp (4) and Rehm (5) modified by Meschia (3) was further simplified (Fig. 1). The two rubber gaskets originally used above and below the membrane were replaced by two "O" rings fitted into corresponding grooves of the Lucite plate and ring, respectively. The capillary glass tubing was replaced by a blunt-ended 15-gauge stainless steel needle anchored to the Lucite plate from below. The needle hub was connected to a Statham pressure transducer. Statham transducer model no. P23Db was used with the large osmometer and Statham model no. SF4 with the small osmometer, the choice being dictated by the fact that the length of time required to reach equilibrium is determined by the volume displacement of the transducer diaphragm and the surface area of the membrane. A recording of the COP was made with a Beckman dynograph using a chart speed of 1 mm/min. The base line was determined with isotonic saline on both sides of the membrane. The saline was replaced by plasma after the base line had remained stable for approximately 30 min. The COP was measured by the deflection from base line to the plateau of the pressure tracing. (Fig. 2). The preparation of the collodion membrane was carried out as described previously (3). The small osmometer had a "working" pore surface of 106 mm^2. Thus, even using a transducer with a very small volume displacement, approximately 30 min was required to reach a plateau as compared with 10–15 min using the large osmometer.

Results. Table I presents the mean plasma colloidal osmotic pressure for 10 adult sheep for comparison with a previous report. It is clear that the modified osmometer used in the present study gives substantially the same results as earlier methods, but does so far more quickly and conveniently. The data for 33 full-term pregnancies of man are also presented in Table I. The mean ± 1 SEM maternal plasma COP (439 ± 9 mm H_2O) was higher than the paired fetal plasma COP (340 ± 7 mm H_2O). This difference was significant ($p < 0.001$), reflecting principally the difference in total protein concentration between fetal and maternal plasmas. Also, the COP/g of protein was slightly higher in maternal plasma. As shown in Fig. 3, earlier in gestation the difference between fetal and maternal plasma protein colloidal osmotic

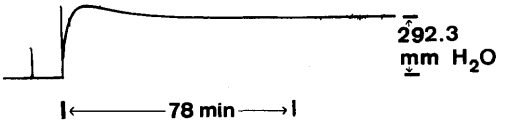

FIG. 2. Measurement of fetal plasma colloidal osmotic pressure illustrating attainment of a plateau after 78 min.

TABLE I. Total Plasma Protein COP.[a]

	COP at 38° (mm H_2O)	Total protein conc (g/100 ml)	COP/g of protein (mm H_2O)
		Adult sheep	
Meschia[b] (7)	372	7.81	48.5
Present work (10)	369 ± 3	7.30 ± 0.08	51.0 ± 0.67
		Man	
Maternal (33)	439 ± 9	7.0 ± 0.11	62 ± 0.91
Fetal (33)	340 ± 7	6.0 ± 0.08	55 ± 0.95

[a] Data presented as mean ± 1 SEM; total no. of observations in each group given in parentheses.

[b] Ref. (3).

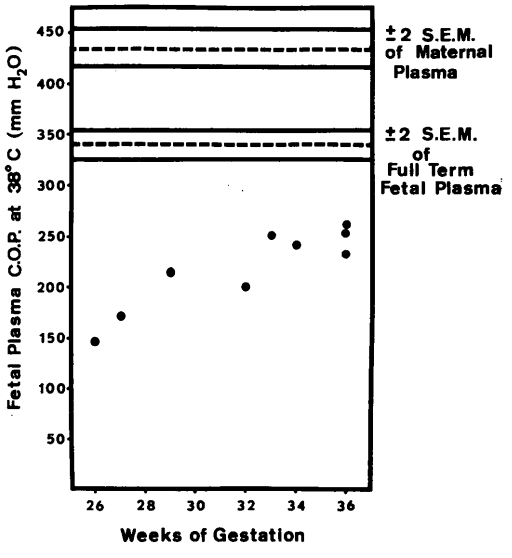

FIG. 3. Fetal plasma colloidal osmotic pressure in man vs gestational age: The maternal and fetal plasma colloidal osmotic pressure at term ± 2 SEM are also shown for comparison.

pressure is much greater. At 26 weeks gestation, the fetal plasma COP was approximately 30% that of the maternal plasma.

Discussion. The only previous study of fetal plasma colloidal osmotic pressure in man, was that of McCarthy. In his study, determinations carried out on diluted sera obtained from six term infants were compared with maternal sera. We have confirmed his finding that in man at term, fetal plasma COP is only slightly lower than maternal plasma COP, ($\Delta\sim$ 90 mm H_2O). This is very similar to the maternal–fetal colloidal osmotic pressure difference described in sheep and goats (1). In fact, it is interesting that at comparable stages in gestation the plasma COP in fetuses of man and sheep were very similar despite marked differences in plasma total protein concentration. The sheep fetus maintains approximately the same plasma colloidal osmotic pressure at a comparable gestational age as the human fetus by having a much higher COP/g of protein, due principally to the presence of fetuin and much lower gamma globulin concentration.

While one might speculate on the possible significance to the fetus of a lower plasma COP, the fact remains that upon delivery, a premature infant must now regulate interstitial and intravascular volumes in the face of a much lower colloidal osmotic pressure than the term infant. This may be one of the reasons why pitting edema is found more frequently in premature than term infants. With the more widespread use of intravenous fluids containing appreciable quantities of sodium in intensive care nurseries, a significant degree of pitting edema is likely to be seen with increasing frequency.

Summary. A rigid membrane osmometer providing a recording of plasma COP within 30 min, is described. The difference between fetal and maternal plasma COP of man at different stages in gestation has been measured. The fetal plasma COP of man increases from approximately 150 mm H_2O at 26 weeks gestation, to approximately 350 mm H_2O at term. The mean maternal plasma COP was 439 ± 9 mm H_2O.

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Abortive Infection of Human Cell Cultures by a Canine Adenovirus (33810)

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Adenovirus replication is usually limited to cell cultures originating from the naturally susceptible host (1). Infection of cells from other species often results in an abortive growth cycle. For example, incomplete replication of human adenovirus 4 in canine cells was described by Carmichael (2). He found that inoculation of canine kidney cells with adenovirus 4 resulted in the synthesis of viral DNA and viral antigens which differed from those produced by adenovirus 4 in human cells. The multiplication cycle was incomplete, since no infectious particles were produced.

Certain exceptions to the incomplete replication of adenoviruses in heterologous cells have been reported. Human adenoviruses have been propagated in cells derived from various animals (3–6). More recently, differences in the abortive cycle of various human adenoviruses in simian cells have been reported (7). These abortive infections resulted in either progressive disappearance of the virus, or in a low-level *de novo* production of infectious particles which never exceeded the input. Replication of several human adenoviruses is enhanced by simian virus 40 or by simian adenovirus 15 in simian cells (8, 9). In these cases a "helper" virus is necessary for adenovirus replication in the heterologous system. Infection of hamster cells by adenovirus 12 results in morphological alteration of the cells (transformation), enhancement of the ability of the cells to divide, and the synthesis of adenovirus 12 specific complement fixing antigens *without infectious virus* (10, 11).

Nonhuman adenoviruses have been propagated in human cells with similar results (12–14). The canine adenovirus, infectious canine hepatitis virus (ICHV), was shown by Govaerts (12) to grow to low titers in several human cell lines when incubated over a period of 4–8 days. More recently, ICHV was shown to be an effective "helper" for the synthesis of adeno-associated virus in human cells (15). The present report describes a nonparallel, *de novo* synthesis of antigens and infectious particles on serial passage of ICHV in human cell cultures.

Materials and Methods. Virus strain. The ICHV was obtained from the American Type Culture Collection and passed once in primary canine kidney cells. It was verified as ICHV by neutralization using rabbit anti-ICHV serum prepared against the Cornell strain.[2]

Cell cultures. Human amnion (HA, strain FL) cells and the Madin Strain of canine kidney cells (MDCK) were used for viral growth. Eagle's minimal essential medium with 10% fetal bovine serum and 0.03% glutamine was used as nutrient medium for the growth of cell monolayers. One hundred units of penicillin and 40 μg of streptomycin/ml were used, and aureomycin (6μg/ml) was

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